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09/980,542	03/04/2002	Nikolay V. Kuchuk	ICON-001	5528

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LERNER, DAVID, LITTENBERG,  
KRUMHOLZ & MENTLIK  
600 SOUTH AVENUE WEST  
WESTFIELD, NJ 07090

EXAMINER

HELMER, GEORGIA L

ART UNIT	PAPER NUMBER
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1638

DATE MAILED: 05/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/980,542

**Applicant(s)**

KUCHUK ET AL.

**Examiner**

Georgia L. Helmer

**Art Unit**

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 12 November 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-36 is/are pending in the application.
- 4a) Of the above claim(s) 25-32 and 36 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-24 and 33-35 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date Nov2001and2004.
- 4) ☒ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. 13 April 2005.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

## **SUPPLEMENTAL DETAILED ACTION**

### ***Restriction election***

1. The Office Action mailed 25 February 2005 is vacated in view of this Supplemental Office Action. The Office acknowledges the receipt of Applicant's restriction election, 12 November 2004. Applicant elects Group I claims, Species [m], claims 1-3, 16 and 33-35, with traverse. Applicant traverses that Groups I and II claims share the same special technical feature (Response, p. 2), that all 36 claims should be examined together, that the restriction to species is also improper for the same reason. Applicant states that Hadley et. al. does not teach methods sharing the same special technical feature as the instant case, and therefore that unity of invention exists for all the claims (Response, p. 4). Applicant had a telephonic interview with Examiners Helmer and Nelson on 13 April 2005, a Summary of which is attached. Applicant's traversal is persuasive in part. The Restriction requirement of 6 October 2004 is amended to withdraw the requirement for species election. Therefore Group I claims 1-24 and 33-35 drawn to method for introducing genetic material into plants, comprising: preparing a first plant transformed with a heterologous nucleic acid having 5' and 3' excisable flanking sequences, crossing a second plant to the transgenic first plant, wherein the first and second plants upon crossing, produce unstable progeny, are examined. Applicant's traversal that all claims should be examined together is unpersuasive. The methods of groups I and II are totally different methods employing different starting materials (Whole plants and plant gametes v. in vitro protoplasts of

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plant cells or plant cells) and different method steps (sexual crosses v. in vitro protoplast fusions).

The claims have been regrouped to correct an inadvertent error in the assignment of claims 33-35. Claims 33-35 are placed in Group I and claims 33-35 deleted from Group II, in accord with the dependency of these claims. Any inconvenience to Applicant is regretted.

To summarize, Group I includes claims 1-24 and 33-35 whereas Group II includes claims 25-32 and 36. Claims 25-32 and 36 are withdrawn as being drawn to a nonelected invention. This restriction is made Final.

***Status of the claims***

2. Claims 1-36 are pending. Claims 1-24 and 33-35 are examined in this action.

***Information Disclosure Statement***

3. Initialed and dated copies of Applicant's IDS form 1449, filed 26 November 2004 and 15 November 2001, respectively, are attached to the instant Office action.

***Claim Rejections - 35 USC § 101***

4. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 34 and 35 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 34 and 35 are drawn to seed, seed parts or progeny from the whole plant containing a heterologous nucleic

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acid. Since the plants and plant material have not been raised under selective conditions, some of the plant material will not be transgenic, rather it will be wild-type, which is a product of nature. Progeny of wild-type tissue are wild-type. Furthermore, due to Mendelian segregation of the transgene, even some progeny of transformed *Allium* will not retain the transgene. See *American Wood v. Fiber Disintegrating Co.*, 90 U.S. 566 (1974), *American Fruit Growers v. Brogdex Co.*, 283 U.S. 2 (1931), *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 33 U.S. 127 (1948), *Diamond v. Chakrabarty*, 206 USPQ 193 (1980

***Claim Rejections - 35 USC § 112-Enablement***

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-24 and 33-35, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant's claims are drawn to a method of introducing genetic material into plants by preparing a first plant transformed with a heterologous nucleic acid having a 5' and 3' excisable flanking sequence that allow movement of said heterologous nucleic acid from one genome to another, crossing a second plant and the transformed first

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plant, wherein said first and second plants, upon crossing produce unstable progeny or demonstrate preferential segregation or sorting out; wherein the excisable flanking sequence comprise a transposable element and the first and second plant produce the compatible transposases, and wherein the excisable flanking sequence comprise a recombination site and the first and second plant produce the compatible recombinase, and selecting progeny of the second plant containing the heterologous nucleic acid . Dependent claims are drawn to the method using specific first and second plants.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands*, 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

Enablement is considered in view of the *Wands* factors (MPEP 2164.01(a)).

*Re the nature of the invention and the breadth of the claims:*

Applicant's invention is a method of introducing genetic material into plants by preparing a first plant transformed with a heterologous nucleic acid having a 5' and 3' excisable flanking sequence that allow movement of said heterologous nucleic acid from one

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genome to another, crossing a second plant and the transformed first plant, wherein said first and second plants, upon crossing produce unstable progeny or demonstrate preferential segregation or sorting out; wherein the excisable flanking sequence comprise a transposable element and the first and second plant produce the compatible transposases, and wherein the excisable flanking sequence comprise a recombination site and the first and second plant produce the compatible recombinase.

*Re the amount of guidance given, and the presence of working examples:*

Applicant gives 5 examples (specification, p. 15-18):

“Example I, Transformation /line conversion of Brassica napus” using *Orychopragmus violaceus* as the first plant and Brassica species as the second plant, including a description of transformation constructs comprising the Spm transposase and related elements. This example says that two independent *Orychopragmus violaceus* transformants containing a single copy insertions have been crossed as male parents to different Brassica, the resulting hybrids selfed and F-1 progeny selected for the presence of the dSPM element, survivors “screened for pure Brassica phenotype, and the absence of GUS activity, and tested finally for the absence of either transposases sequence or species specific *Orychopragmus* repeats. Finally cosegregation of dSpm with a Brassica chromosome specific RFLP pattern has been establishing by analyzing the F2 progeny (specification p. 17).

“Example II, Transformation /line conversion of Brassica napus” using *Orychopragmus* the first plant and Brassica species as the second plant, using the

method of DeBlock, 1989, sets forth that two independent transformed plants of each species were selected based on molecular analysis of the transgenics, crosses and analysis of progeny as Example II.

“Example III, Transformation /line conversion of potato” using *Arabidopsis thaliana* as the first plant and Potato as the second plant, using the crossing method of Hermesen, 1973, and primary converted lines selected as F0 diploidized dihaploids.

“Example IV, Transformation /line conversion of maize” using *Tripsacum dactyloides* as the first plant and maize as the second plant, using the method of Hiei, et. al., 1997, wherein transgenic plants were crossed with maize varieties, resultant progeny selfed, pure maize-type segregates were screened from the BC1 by PPT resistance or PCR analysis...and cosegregation of PPT resistance or specific PCR signals with maize chromosome-specific RFLP pattern was established by analyzing the BC/F2 progeny.

“Example V, Transformation /line conversion of wheat”, performed as in Example IV except that the crosses were done as taught by Riera-Lizarazu et. al., 1993, and that primary converted lines were selected as F0 diploidized haploids emerging from the crosses.

Each of these Examples includes only very rudimentary experimental details and closes with statements to the effect that the transformation was done, crosses were done, and progeny were selected. No details of what, if any, of the examples produced any of the desired progeny, having the desired heterologous nucleic acid transferred from the first plant to the second plant.

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No information is given on any of the putative Spm transformants and related heterologous nucleic acid transferred. No examples are given of any recombinase, wherein the excisable flanking sequence comprise a recombination site and the first and second plant produce the compatible recombinase. The claimed invention is not exemplified.

The predictability of the art or lack thereof:

Re *sexually crossing any plant, where plants are of different species*: Applicant claims the transformation /line conversion by crossing a first plant and a second plant wherein the first and second plant are not in the same Genus or species.

Applicant gives no information on which, if any, of the progeny produce the claimed transgenic progeny. Species are groups of potentially interbreeding natural populations which are reproductively isolated from other such groups (Rieger et al., Glossary of Genetics & Cytogenetics, 1976, Springer-Verlag, NY, page 511). The state of the art is that such at one skilled in the art can readily do sexual crosses within the species, with reasonable expectation of success of hybrid progeny. However, the interspecific cross is difficult to make and the hybrid that is produced is often inviable or sterile (Hadley et. al., in Hybridization in Crop Plants, ed. Fehr & Hadley, Society of Agronomy and Crop Science Society of America, Madison, Wisconsin, page 133). Applicant has provided no guidance on how to predictably eliminate inoperable embodiments from a virtually ad infinitum of possibilities other than by random trial and error, which is excessive experimentation and an undue burden. Without further guidance, one of skill in the art would be required to do many experiments involving a

myriad of combinations. This would impose a burden on the skilled artisan, without a reasonable expectation of success.

*Re the recombinase:* Applicant claims any and all recombinases, and use of all recombinases in the claimed invention. Applicant gives no information or guidance with respect to the use of the specific recombinase system. Site-specific recombinase are very complex enzyme systems where the recombinase has several functions—namely, recognition of recombination sites, cleavage of recombination site at specific cleavage sites, strand swapping to produce the recombinant strand, and ligation to produce the reconfigured product. It is unpredictable that any and all recombinases, would properly perform all the above functions. Applicant has provided no guidance on how to predictably eliminate inoperable embodiments from a virtually ad infinitum of possibilities other than by random trial and error, which is excessive experimentation and an undue burden. Without further guidance, one of skill in the art would be required to do many experiments involving a myriad of combinations. This would impose a burden on the skilled artisan, without a reasonable expectation of success.

*Re generation a haploid transgenic plant:* This process needs to have had the following events occur successfully and in the proper sequence for such generation:

- Sexual crossing
- providing the recombinase,
- generating a haploid cell/plant.

For formation of a hybrid cell of a first plant and a second plant, chromosome pairing and recombination occurring between chromosomes of a second plant and a first plant

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p in such a manner as to produce recombination at non-identical sites and insert nucleotide sequence of interest at a target site, production of haploid cell, culturing of cell(s)/tissue to produce a hybrid transgenic plant. A number of issues need to be addressed successfully for this process to occur: synthesis of the hybrid, chromosome pairing and genetic recombination. Of issue in wheat/maize hybridization, are crossability of the parents, and specific genotypes of the parents to be used, among other factors, as discussed by Jauhar, et. al. Chromosome-mediated and direct gene transfers in wheat, *Genome* 42: 570-583, 1999, pages 572-3.

The chromosomes need to pair and recombination occur to produce the desired product. Recombination occurs upon such time as the recombinase is provided and catalyses the various recombinase events. The recombinase needs to be provided at the proper time, in the proper place, at an adequate concentration, at the proper phase of the cell cycle, for the proper duration of time for the desired recombination event(s) to occur. For the site-specific recombinases, the recombination event is reversible. Since the wild-type recombination sites readily recombine with each, the proper conditions for catalysis need to be determined for the successful event to occur. Embryo rescue is necessary for haploid production from wheat x maize hybrids (Zhang, et. al., *Wheat embryogenesis and haploid production in wheat x maize hybrids*, *Euphytica* 90: 315-324, 1996, p 315. ). Proper conditions for this need to be determined. Once transgenic haploid cell(s) are produced, progeny needs to be generated.

While working examples are not required, Applicant must provide sufficient guidance to address these issues discussed above. Without such guidance, the

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experimentation required would not be routine, but would be undue. Applicant has provided no guidance on how to predictably eliminate inoperable embodiments from a virtually ad infinitum of possibilities other than by random trial and error, which is excessive experimentation and an undue burden. Without further guidance, one of skill in the art would be required to do many experiments involving a myriad of combinations. This would impose a burden on the skilled artisan, without a reasonable expectation of success.

*Experimentation required:* Undue experimentation would be required to determine which **combinations and sequence of the various steps** would function to produce the claimed invention. For example, what recombinase, of the many available such as the site-specific recombinases systems FLP/FRT, Cre/lox, R/Rx would function as desired for the movement of a heterologous nucleic acid from a chromosome of one genome of one species to a chromosome of the genome of a second species. The recombinase needs to be provided at the proper time, in the proper place, at an adequate concentration, at the proper phase of the cell cycle, for the proper duration of time for the desired recombination event(s) to occur. Determining the specific combinations and sequences of the various steps which would function to produce the claimed invention would require a number of independent sets of experimentation. Experimentation would need to determine which recombinases, in which parental plants, in what transgenic construct, with what kind of regulatory sequences for expression of the recombination partners, be such expression sequence tissue specific, cell cycle dependent, or developmental stage specific, would function to produce the

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claimed invention. There are an infinitely large number of combinations of regulatory sequences for coding sequences and a number of possible recombinases; these factors alone would require an exceeding large number of sets of experiments to determine which ones would function as desired. Applicant must provide sufficient guidance to address these issues. Without such guidance the experimentation required would not be routine, but would be undue. This would impose a burden on the skilled artisan, without a reasonable expectation of success.

In view of the breadth of the claims (sexually crossing any first plant with any second plant of different genus and species of any genotype, any recombinase, and any transposase) and the lack of guidance in the specification, undue experimentation would be required to enable the invention as commensurate in scope with the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

***Remarks***

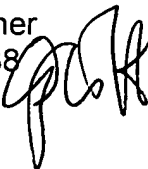
7. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Georgia L. Helmer whose telephone number is 571-272-0796. The examiner can normally be reached on 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 571-272-0804. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Georgia Helmer PhD  
Patent Examiner  
Art Group 1638  
May 19, 2005



AMY J. NELSON, PH.D  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600